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REMARKS

§102(e) Rejection

Claims 1-3 and 5-9 were rejected under 35 U.S.C. §102(e) as being unpatentable over Kim *et al*, U.S. Patent No. 5,648,225 ("Kim"). (Paper no. 22, para. 5). For the reasons presented below, however, reconsideration and withdrawal of the rejection respectfully is solicited.

Kim discloses a multipurpose reagent for rapid analysis of a whole blood sample. (Abstract). The reagent is used to analyze white blood cells. (Example 1). Monoclonal antibodies (CD 3,4, 8 and 19) are added to the reagent for the analysis of lymphocytes. (See Column 8, line 66 to Column 9, line 48, and Example 2). The reagent is mixed with a nuclear stain for the analysis of red blood cells. (See Column 8, line 38, and Example 5).

The Examiner contends that all of the Applicants' claim limitations "are disclosed for the same use or purpose in flow cytometry." (Final Office Action, para. 4(a), p. 4) Even accepting this proposition, *arguendo*, (although Applicants respectfully disagree with it) even this does not render Applicants' claims anticipated. As Applicants reiterate, nowhere does Kim disclose adding or using *both* monoclonal antibodies and nuclear stains in the same method, as Applicants' claim.

This is fatal to the rejection because, as Applicants have stated previously, Anticipation under §102 requires "identity of invention." *Glaverbel Societ Anonyme v. Northlake Mktg. & Supply.*, 33 USPQ2d 1496, 1498 (Fed. Cir. 1995). Aggregate inclusion of separate elements claimed by the Applicants without disclosing their interrelation, as in the claim, is insufficient. Again the law is clear, each and every element recited in a claim must be found in a single prior art reference and **arranged as in the claim**. *In re Marshall*, 198 USPQ 344, 346 (CCPA 1978); *Lindeman Maschinenfabrik GMBH v. American Hoist and Derrick Co.*, 221 USPQ 481, 485 (Fed. Cir. 1984).

Claim 1 does not
explicitly
include
monoclonal antibodies
1
Kim does not describe that monoclonal antibodies are used for the analysis of erythroblasts, and does not describe or suggest that a mixture of the nuclear stain and the monoclonal antibodies **are used in one analytical reagent or method**. Kim does not teach, disclose or suggest that the nuclear stain and the monoclonal antibodies can exist together, let alone used together. This is far from an "identity of invention." Withdrawal of the rejection is respectfully solicited.

§103(a) Rejection

Claims 4 and 10-13 were rejected under 35 U.S.C. §103(a) as being unpatentable over Kim and Inami et al., U.S. Patent No. 5,298,426 ("Inami"). (Paper no. 22, para. 6). For the reasons presented below, however, reconsideration and withdrawal of the rejection respectfully is solicited.

Applicants previously argued that the combination of references fail to disclose the affirmative manipulative steps taken with respect to the two signal types, i.e. nucleotide fluorescent and fluorescent labeled antibody signals, appearing in Applicants' claims. While the

Examiner contends that these gaps are filled by the combination of Kim and Inami, nothing in these citations discloses acting upon these two signals together according to Applicants' method claims. Therefore, at the very least, the Applicants' claimed steps of detecting, analyzing, and discriminating *between these two signals*, are necessarily absent and the Examiner's rejection improperly fails to account for them.

The Examiner's response to this argument in the Final Office Action misses the point. The Examiner considers these steps to be "clearly inherent." Fundamentally, to reject claims to a method, the references relied upon by the Examiner must account for the manipulative steps claimed. *In re Magat*, 112 USPQ 317, 319 (CCPA 1957). Here, the manipulative steps of Applicants' claims act on two signals, and neither Kim nor Inami discloses manipulative steps to discriminate between these two signals. Amalgamating the disclosure in the citations to meet Applicants' claims, must, by necessity, involve speculation beyond the disclosure of the two references. And no facts or evidence adduced supports such an amalgam.

As such, the Examiner's rejection falls far short of providing the requisite motivation to deviate from Kim to arrive at the claimed invention. The citations must "suggest the desirability of the combination" that is claimed. See MPEP 2143.01 at 2100-110, 111 and MPEP 2145 (j) 3 at 2100-127. This MPEP section further requires that "Obviousness can only be established by combining or modifying the teaching of the prior art to produce the claimed invention where there is *some teaching, suggestion or motivation* to do so..." (Emphasis added). No teaching, suggestion or motivation in Kim or Inami supports any modification of the disclosures therein to arrive at what the Applicants have claimed.

Apparently undaunted by these requirements, the Examiner nonetheless provides her own teaching, suggestion or motivation, all entirely absent from the citations. For instance, the Examiner states the following:

"Given the combined teaching of both Kim and Inami, where appropriate reagents and concentrations thereof are used, all of detection, analysis, and discrimination between the desired populations using measurements of fluorescence intensities or fluorescent signals, manipulation of results obtained, and population distribution in a histogram are precisely the power of flow cytometric analysis." (Final Office Action, para. 4(c), p. 6.)

The Examiner cites to no specific disclosure from Kim or Inami to support this statement. There is no support for an "appropriate" reagent, (nor is a definition of such apparent) nor is any support provided for what may be the "power of flow cytometric analysis."

The Examiner states further:

"It would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute the buffer solution of Kim with the two reagent system taught by Inami for use in permeabilizing erythroblasts because Kim specifically taught that integrity and antigenicity of white blood cells need to be optimally maintained during permeabilization, i.e. lysing, of the nRBC's or erythroblasts on order to allow accurate simultaneous quantitation of both populations and Inami specifically taught that the two reagent system eliminates lysing conditions for erythroblasts while maintaining the integrity and shape of WBCs for accurate differentiation of both erythroblast and leucocyte populations." (Final Office Action, para. 4(c), p. 6)

Yet, nowhere does Kim teach, suggest or disclose that its buffer solution would operate in other reagent systems, let alone the two reagent system of Inami. No facts or evidence adduced supports the alleged modification of Kim. In addition, even if Kim may be read to generally teach that WBC integrity need to be optimally maintained, no evidence supports a teaching, suggestion or motivation for modifying Kim specifically by substitution with the method of Inami, as apart from any other methods that may accomplish the same, to result in the

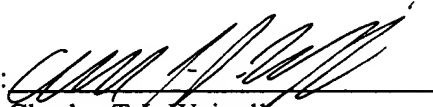
Applicants' specific claims. Thus, no facts or evidence supports the alleged motivation to modify Kim. Also, if Inami teaches a two reagent system that eliminates lysing conditions, this does not teach, suggest or motivate the incorporation of the Kim buffer solution. Thus, no facts or evidence supports the alleged motivation to modify Inami. In sum, taking Kim and Inami and their disclosures, the citations do not encompass the Applicants' specific claim limitations and, furthermore, one does not arrive at Applicants' specific claims without improper hindsight analysis. Simply put, the bases for the rejection are clearly insufficient.

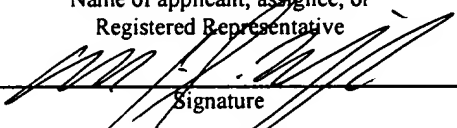
Other deficiencies in the Examiner's §103 rejection are plain and have been argued previously. For instance, Applicants' have already demonstrated that Kim does not teach analysis of a particular sample using both 1) erythroblast nucleotide dye staining and 2) leukocyte cell surface marker fluorescent labeling, whether such use is simultaneous or otherwise. Hence, Claim 1, from which the other claims ultimately depend, is not anticipated by Kim, hence Kim is not a proper primary citation for the obviousness rejection. Inami, does not, further, remedy these deficiencies in the disclosure of Kim. In addition, the Examiner also specifically acknowledged that "Kim and Inami are silent in disclosing differentiating between different stages of erythroblast populations," as recited in Claim 10, and as is incorporated, by their dependency on Claim 10, into Claims 11 and 12.

In sum, the Examiner has not adduced factual support demonstrating the requisite motivation for the combination of references advanced against Applicants' claims. In addition, the citations fail to account for all the Applicants' claim limitations and lack any disclosure motivating their combination. The Examiner has not met her burden of demonstrating a *prima facie* case of obviousness, therefore, the rejection should be withdrawn.

In view of the foregoing, favorable action on the merits, and allowance of all claims, respectfully is solicited.

Respectfully submitted,

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